

**REMARKS****Status of the Claims**

Claims 1 to 31 were acted upon by the Examiner in the Office Action dated March 9, 2005. A Reply under 37 C.F.R. §1.115 to Final Office Action was filed July 11, 2005. In response, an Advisory Action, dated July 29, 2005 was forwarded by the Examiner. Claims 1 to 31 have been rejected. The amendments to claims 2 to 24 submitted in the Reply dated July 11, 2005 have not been entered. In response, applicants are submitting herewith a Request for Continued Examination.

Applicants respectfully request that the amendments submitted with the Reply dated July 11, 2005 not be entered. Instead, applicants request that the amendments submitted herewith be entered.

Claims 1 to 31 have been rejected. Claims 1, 3, 7, 22, and 26 to 31 have been amended. Claims 2, 6, 14 to 17, 19 to 21, and 25 have been canceled. Claim 34 has been added. Accordingly, claims 1, 3 to 5, 7 to 13, 18, 22 to 24, 28 to 31, and 34 are presented for examination.

**Summary of the Examiner's Action****Claim Rejections**

Claims 1, 3 to 5, 22, and 26 to 28 stand rejected under 35 U.S.C. §102(a), as being anticipated by Crespo (WO 97/33975, wherein the English version is US 6,248,588).

Claims 1, 7 to 13, 22 to 24, 26 and 29 to 31 stand rejected under 35 U.S.C. §103(a), as being unpatentable over Crespo in view of Engler (US 2003/0211598).

Claims 1, 3 to 5, 7 to 13, 18, 22 to 24, 26 to 31 stand rejected under 35 U.S.C. §103(a), as being unpatentable over Crespo taken with Engler and further in view of Rolland (US 6,040,295) or Sene (WO 98/02522, wherein its English version is US 6,451,256).

Applicants respectfully traverse the Examiner's rejection.

**Discussion****Amendments to the Claims**

Applicants have amended claim 1 to recite "A recombinant adenovirus vector or particle storage composition comprising Tris-HCl, and about 0.01% to about 25%, human serum albumin

(HSA), wherein the pH of said composition is greater than or equal to 5.0 and less than or equal to 9.0, said composition effective to enhance the titer of the adenovirus vector or particle stored at about 4°C to about +20°C for at least about 3 months to about 8.5 months".

Support for the recitation of "Tris-HCl" is found in originally filed claim 14. Support for the recitation "about 0.1% to about 25%" is found in originally filed claim 2. Support for the recitation "pH of said composition is greater than or equal to 5.0 and less than or equal to 9.0" is found in originally filed claim 6. Support for the recitation "enhance the titer" is found on page 6, line 4 of the application. Support for the recitation "stored at about 4°C to about 20°C for at least about 3 months to about 8.5 months" is found Example 6 (page 33, line 29 to page 36, line 13) and Figure 11 of the application.

#### Discussion of the Section 102(a) Rejections

Claims 1, 3 to 5, 22 and 26 to 28 have been rejected under 35 U.S.C. §102(a) as being anticipated by Crespo (WO 97/33975, wherein the English version is US 6,248,588).

Applicants respectfully traverse the rejection.

Claims 1, from which the other rejected claims depend, has been amended to recite a "composition comprising Tris-HCl". As noted by the Examiner on page 5 of the Action dated March 9, 2005, Crespo does not teach a Tris-HCl buffer. In addition, column 10, lines 26 to 30, of Crespo recites:

A medium according to the invention allows the freezing and thawing of biological material under conditions of high viability. The media according to the invention may, in particular, allow the freezing of biological material at temperatures of between -200 and -4 degrees Celsius.

Accordingly, as indicated also by the claims and abstract of Crespo, Crespo discloses a solution for freezing adenovirus. The presently amended claims are directed to compositions used above freezing temperatures (4°C to 20°C).

Thus, Crespo does not teach elements of the presently claimed invention, applicants respectfully request that the rejection of claims 1, 3 to 5, 22, and 26 to 28 under 35 U.S.C. §102(a) as being anticipated by Crespo be withdrawn.

**The 35 U.S.C. §103(a) Rejections**

Claims 1, 7 to 13, 22 to 24, 26 and 29 to 31 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Crespo in view of Engler et al. (US 2003/0211598).

Engler et al. discloses delivery-enhancing buffers comprising a detergent or ethanol. Engler et al. has been cited for disclosure of Tris buffers. The Examiner asserts that the combination of Crespo and Engler et al. render the presently claimed invention obvious.

Applicants respectfully traverse the rejection.

With regard to a *prima facie* obviousness rejection, MPEP §2143 states:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Accordingly, a proper *prima facie* case of obviousness requires three steps: 1) providing a suggestion or motivation to combine the references; 2) providing a reasonable expectation that the combination will be successful; and 3) providing a combination that teaches all of the claim limitations. Steps 1) and 2) must be found in the prior art. Applicant submits that the present rejection has not satisfied any of these requirements.

For the reasons noted above, Crespo does not disclose compositions useful for preserving adenoviral particles or vectors at temperatures above freezing and there is no evidence to suggest that the compositions of Crespo would be effective at these temperatures. In contrast, the presently claimed invention is effective at temperatures from about 4°C to about 20°C. The teachings of Engler et al., which relate to delivery-enhancing agents, provide no basis to overcome the deficiencies of Crespo. Accordingly, the Examiner has not satisfied the third requirement of teaching or suggesting all the claim limitations.

Furthermore, as noted in MPEP §2143, the suggestion or motivation to combine the references and the reasonable expectation that the combination will be successful must be found in the prior art. The Examiner has provided no indication of why one skilled in the art would

combine a cryopreservation publication with a delivery-enhancing agent and why such a combination would be successful. Accordingly, the Examiner has not satisfied any of the requirements of a *prima facie* case of obviousness.

In addition, applicants submit that the present invention is nonobvious in view of the objective evidence presented below.

MPEP §2141 states (emphasis added):

Objective evidence or secondary considerations such as unexpected results, commercial success, long-felt need, failure of others, copying by others, licensing, and skepticism of experts are relevant to the issue of obviousness and must be considered in every case in which they are present. When evidence of any of these secondary considerations is submitted, the examiner must evaluate the evidence.

Accordingly, MPEP §2141 requires that objective evidence such as unexpected results be considered when evaluating whether an invention is obvious. In the present application, Figure 11 on page 43 of the application provides such evidence. Figure 11 depicts results wherein the presently claimed composition maintains the titer of adenoviral particles up to about 8.5 months at 4°C and 20°C. Such results would not be expected by one of skill in the art upon reviewing Crespo (directed to freezing solutions) and Engler et al. (directed to delivery-enhancing agents). Indeed, there are no disclosures in the prior art, including Crespo and Engler et al., that are predictive of this dramatic and unexpected viral stability at these increase temperatures.

Accordingly, applicants respectfully request that the rejection of claims 1, 7 to 13, 22 to 24, 26 and 29 to 31 under 35 U.S.C. §103(a) as being unpatentable over Crespo in view of Engler et al. be withdrawn.

Claims 1, 3 to 5, 7 to 13, 18, 22 to 24, 26 to 31 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Crespo taken with Engler et al. and further in view of Rolland et al. (US 6,040,295) and Sene (WO 98/02522, wherein the English version is US 6,451,256).

Applicants respectfully traverse the rejection.

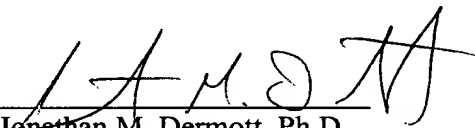
Rolland et al. discloses compositions and methods for enhancing the uptake of nucleic acids by cells or organisms. Sene discloses methods for preserving viral particles in a sucrose solution.

For the reasons noted above, the combination of Crespo and Engler et al. are non-obvious. Rolland et al. and Sene provide no basis to overcome these deficiencies. Accordingly, applicants respectfully request that the rejection of claims 1, 3 to 5, 7 to 13, 18, 22 to 24, 26 to 31 under 35

U.S.C. §103(a) as being unpatentable over Crespo taken with Engler et al. and further in view of Rolland et al. and Sene be withdrawn.

A favorable action on the merits is requested respectfully. A Petition for a three-month extension of time, from June 9, 2005 to September 9, 2005, is enclosed. The fee for a one-month extension was paid with the Reply filed July 11, 2005. Accordingly, the fee for the present three-month extension has been reduced by this amount.

Respectfully submitted,

  
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